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For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: ANTIBODIES DERIVED FROM ANTI ED-B L19 AND TARGETING TUMOR VASCULATURE

(57) Abstract: The present invention relates to selectively targeting tumoral vasculature in vivo using a human recombinant scFv, L19, to the angiogenesis marker ED-B domain of fibronectin. In preferred embodiments, a complete human IgG1 is employed having the variable regions of L19. In other embodiments is employed a mini-immunoglobulin generated by fusing the scFv L19 to the constant CH4 domain of a secretory IgE isoform that naturally contains a cysteine in its COOH terminal and which forms a covalently linked dimer. Different in vivo behaviour of the antibody formats is exploitable for different diagnostic and/or therapeutic purposes, depending on clinical needs and disease. The antibody molecules may be labelled as described.

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# INTERNATIONAL SEARCH REPORT

Internat. Application No.  
PCT/IB 03/01458

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/46 C07K16/18 A61K51/10 G01N33/68 C12N1/21  
C12N15/13 A61K39/395 A61P9/00 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99 58570 A (EIDGENOSSISCHE TECHNISCHE HOCHSCHULE ZURICH, SWITZ.) 18 November 1999 (1999-11-18) claims 1-27	1-9, 13-26
Y	EP 1 130 099 A (CRUCCELL HOLLAND B V) 5 September 2001 (2001-09-05) claims 1-44	1-4, 9-26
Y	WO 94 09817 A (CITY OF HOPE) 11 May 1994 (1994-05-11) claims 1-16; figure 2; examples 1,2	1,5-8
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

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## INTERNATIONAL SEARCH REPORT

Internat. Application No

IB 03/01458

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LI ERQIU ET AL: "Mammalian cell expression of dimeric small immune proteins (SIP)." PROTEIN ENGINEERING, vol. 10, no. 6, 1997, pages 731-736, XP002252049 ISSN: 0269-2139 cited in the application abstract; figures 1,2 ---	1,5-8
Y	WO 01 62800 A (EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZURICH, SWITZ.) 30 August 2001 (2001-08-30) page 4, line 5 -page 5, line 15; examples 2-7; table 1 claims 1-34 ---	1,10-12
A	BATISTA F D ET AL: "The two membrane isoforms of human IgE assemble into functionally distinct B cell antigen receptors." THE JOURNAL OF EXPERIMENTAL MEDICINE. UNITED STATES 1 DEC 1996, vol. 184, no. 6, 1 December 1996 (1996-12-01), pages 2197-2205, XP002252050 ISSN: 0022-1007 cited in the application the whole document ---	1-26
A	PINI A ET AL: "Design and use of a phage display library. Human antibodies with subnanomolar affinity against a marker of angiogenesis eluted from a two-dimensional gel" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, no. 34, 21 August 1998 (1998-08-21), pages 21769-21776, XP002124781 ISSN: 0021-9258 cited in the application page 21774, left-hand column, line 7 -page 21775, left-hand column, line 32; table II ---	1-26
E	WO 03 055917 A (SCHERING AKTIENGESELLSCHAFT, GERMANY) 10 July 2003 (2003-07-10) page 4, line 28 -page 5, line 2 page 17, line 8 -page 19, line 6 claims 1-21; table 1 --- -/--	1-26

## INTERNATIONAL SEARCH REPORT

Internat I Application No

/IB 03/01458

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>BORSI LAURA ET AL: "Selective targeting of tumoral vasculature: comparison of different formats of an antibody (L19) to the ED-B domain of fibronectin." INTERNATIONAL JOURNAL OF CANCER. JOURNAL INTERNATIONAL DU CANCER. UNITED STATES 1 NOV 2002, vol. 102, no. 1, 1 November 2002 (2002-11-01), pages 75-85, XP002252051 ISSN: 0020-7136 the whole document</p>	1-26

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB 03/01458

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 18,19 and 21 could comprise a diagnostic method practised on the human/animal body or could be directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat'l Application No

T/IB 03/01458

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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